

REMARKS

Applicants thank the Examiner for acknowledging and entering Applicants' amendment of January 11, 2007. Applicants also thank the Examiner for reconsidering claims 99-101 that depend directly or indirectly from allowed independent claim 21 and including them in the instant restriction requirement.

Applicants now amend the claims to reflect an election required by the April 4, 2007, Office Action, as well as to clarify that the process claims (claims 43, 109-113, 119-126 and new claims 127-143) require all limitations of product claims 28 or 40. In addition, claims 114-117 are canceled, as redundant in view of the new claims. There is no issue of new matter.

In the April 4, 2007 Action, the Examiner required restriction under 35 U.S.C. §121 between:

- Group I. Claims 21, 28, 40, 99-104, 106-108, allegedly drawn to a vector and a mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate; and
- Group II. Claims 43, 109-117, 119-126, allegedly drawn to a method of changing a target sequence in genomic DNA of a mammalian cell.

Applicants elect Group I for further prosecution in this application, corresponding to claims 21, 28, 40, 99-104 and 106-108. This election is made without traverse.

In addition, Applicants respectfully submit that the withdrawn and new process claims require all limitations of elected product claims 28 or 40, as clarified by the amendment made herewith. Specifically, independent amended process claim 43 contains all limitations of claim 28; independent new process claim 127 contains all limitations of claim 40; and the remaining process claims depend either directly or indirectly from claims 43 or 127.

To better demonstrate this, claim 28 and amended claim 43 are reproduced below, with corresponding language italicized:

28. **(Previously presented)** *A mammalian cell comprising:*
- (a) *a chimeric nuclease; and*
 - (b) *a repair substrate, wherein the chimeric nuclease comprises:*
 - (i) *a nuclear localization signal;*
 - (ii) *a DNA binding domain; and*
 - (iii) *a cleavage domain,*
- and wherein the repair substrate comprises:*

(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and

(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

43. **(Withdrawn and Currently amended)** A method of changing a target sequence in ~~genomic~~ chromosomal DNA of a mammalian cell, comprising:

(a) introducing a chimeric nuclease, ~~or nucleic acid encoding the chimeric nuclease~~, into the cell, wherein said chimeric nuclease comprises:

(i) a DNA binding domain;

(ii) a cleavage domain; and

(iii) a nuclear localization signal; and

(b) introducing a repair substrate into the cell, wherein said repair substrate comprises:

(i) a nucleic acid sequence that is substantially identical to a region ~~surrounding~~ flanking the target sequence; and

(ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,

whereby the target sequence is changed by the repair substrate upon recombination.

Similarly, new process claim 127 requires all limitations of elected product claim 40 as demonstrated below:

40. **(Previously presented)** A mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate, wherein the chimeric nuclease comprises:

(i) a nuclear localization signal;

(ii) a DNA binding domain; and

(iii) a cleavage domain,

and wherein the repair substrate comprises:

(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and

(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

127. (New) A method of changing *a target sequence in chromosomal DNA* of a mammalian cell, comprising:

(a) introducing *a nucleic acid encoding a chimeric nuclease* into the cell, wherein said chimeric nuclease comprises:

- (i) *a DNA binding domain;*
- (ii) *a cleavage domain; and*
- (iii) *a nuclear localization signal;*

whereby the chimeric nuclease is produced in the cell; and

(b) introducing *a nucleic acid comprising a repair substrate* into the cell, wherein said repair substrate comprises:

- (i) *a nucleic acid sequence that is substantially identical to a region flanking the target sequence; and*
- (ii) *a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,*

whereby the target sequence is changed by the repair substrate upon recombination.

As acknowledged by the Examiner on page 3 of the Action, allowance of the product claims will entitle Applicants to consideration of withdrawn process claims depending from or *otherwise requiring all limitations* of the allowable claims (our emphasis). As demonstrated above, non-elected process claim 43 requires all limitations of product claim 28 and new process claim 127 requires all limitations of product claim 40. Further, as stated above, the other withdrawn claims of Group II depend either directly or indirectly from claim 43, while newly added claims 128-143 depend either directly or indirectly from new claim 127, thus also requiring all limitations of claims 28 or 40.

Accordingly, Applicants make the present election with the understanding that the finding of claims 28 and 40 allowable entitles Applicants to automatic rejoinder of the withdrawn Group II claims in accordance with M.P.E.P. §821.04, as well as automatic rejoinder of the newly added claims. In addition, Applicants reserve the right to pursue the subject matter of the non-elected invention at a later date, for example, in continuing or divisional applications.

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CONCLUSION

Elected claims 21, 28, 40, 102-104 and 106-108 remain allowed, according to the October 6, 2006 Office Action. Applicants again respectfully submit that elected product claims 99-101 depend directly or indirectly from allowed independent claim 21 and further respectfully submit that non-elected process claims 43, 109-113 and 119-126, as currently amended, as well as new process claims 127-143, require all limitations of claim 28 or claim 40. Accordingly, Applicants request timely allowance of all the elected claims, as well as automatic rejoinder of all the non-elected and new claims.

If a telephone call will help expedite any aspect of the prosecution of the instant application, Applicants encourage the Examiner to contact the undersigned by telephone at (415) 568-2257 or by fax at (415) 568-2260.

Respectfully submitted,
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Dated: _____

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